

Amendments to the Specification:

Please replace the paragraph beginning on page 1, line 27 and ending on page 1, line 34 with the following amended paragraph:

This application is a continuation application filed under 37 C.F.R. § 1.53(b) of application number 09/874,514, filed June 5, 2001, which is a continuation application filed under 37 C.F.R. § 1.53(b) of application number 08/986,025, filed December 3, 1997, and issued as U.S. Patent No.: 6,242,469 on June 5, 2001, the entire contents of which are hereby incorporated by reference, which is based on U.S. Provisional Application Serial Nos. 60/032,282, 60/033,767, 60/047,566, 60/047,941, and 60/055,533, filed December 3, 1996, January 14, 1997, May 22, 1997, May 29, 1997, and August 13, 1997, respectively, the contents of which are hereby incorporated by reference into this application. This invention was made with government support under grants CA-28824, CA-39821, CA-GM 72231, CA-62948, and AI0-9355 from the National Institutes of Health, and grant CHE-9504805 from the National Science Foundation. Additionally, the present invention was supported in part by a fellowship from the United States Army to Dongfang Meng (DAMD 17-97-1-7146), and thus the government has certain rights in the invention.

Please replace the paragraph beginning on page 3, line 21 and ending on page 3, line 22 with the following paragraph:

~~Figure 3(A) provides~~ Figures 3(A) and 3(B) provide syntheses of key iodinated intermediates used to prepare hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives.

Please replace the paragraph beginning on page 3, line 24 and ending on page 3, line 27 with the following paragraph:

~~Figure 3(B) provides~~ Figures 3(C) and 3(D) provide methods of preparing

hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives, said methods being useful generally to prepare 12,13-E epothilones wherein R is methyl, ethyl, n-propyl, and n-hexyl from the corresponding E-vinyl iodides.

Please replace the paragraph beginning on page 3, line 29 and ending on page 3, line 30 with the following amended paragraph:

~~Figure 3(B) shows~~ Figures 3(E) and 3(F) show reactions leading to benzoylated hydroxymethyl-substituted desoxyepothilone and hydroxymethylene-substituted epothilone (epoxide).

Please replace the paragraph beginning on page 4, line 9 and ending on page 4, line 9 with the following amended paragraph:

~~Figure 6 provides~~ Figures 6(A) and 6(B) provide a scheme of an olefin metathesis route to epothilone A and other analogues.

Please replace the paragraph beginning on page 4, line 29 and ending on page 4, line 29 with the following amended paragraph:

~~Figure 14 shows~~ Figures 14(A) and 14(B) show the preparation of intermediate 4A.

Please replace the paragraph beginning on page 5, line 7 and ending on page 5, line 8 with the following amended paragraph:

~~Figure 18 provides~~ Figures 18(A) and 18(B) provide a synthetic pathway to a protected intermediate for 8-desmethyl deoxyepothilone A.

Please replace the paragraph beginning on page 5, line 10 and ending on page 5, line 11 with the following amended paragraph:

~~Figure 19 provides~~ Figures 19(A), 19(B), and 19(C) provide a synthetic pathway to 8-desmethyl deoxyepothilone A and a trans-iodoolefin intermediate thereto.

Please replace the paragraph beginning on page 5, line 13 and ending on page 5, line 22 with the following paragraph:

~~Figure 20 shows (top)~~ Figure 20(A) shows structures of epothilones A and B and 8-desmethylepothilone and ~~(bottom)~~ Figure 20(B) shows a synthetic pathway to intermediate TBS ester **10** used in the preparation of desmethylepothilone A. (a) (Z)-Crotyl-B[(-)-lpc]₂, -78°C, Et₂O, then 3 N NaOH, 30% H₂O₂; (b) TBSOTf, 2,6-lutidine, CH₂Cl₂ (74% for two steps, 87% ee); (c) O₃, CH₂Cl₂/MeOH, -78°C, then DMS, (82%); (d) t-butyl isobutyrylacetate, NaH, BuLi, 0°C, then **6** (60%, 10:1); (e) Me₄NBH(OAc)₃, -10°C (50%, 10:1 α/β) or NaBH₄, MeOH, THF, 0°C, (88%, 1:1 α/β); (f) TBSOTf, 2,6-lutidine, -40°C, (88%); (g) Dess-Martin periodinane, (90%); (h) Pd(OH)₂, H₂, EtOH (96%); (i) DMSO, oxalyl chloride; CH₂Cl₂, -78°C (78%); (j) Methyl triphenylphosphonium bromide, NaHMDS, THF, 0°C (85%); (k) TBSOTf, 2,6-lutidine, CH₂Cl₂, rt (87%).

Please replace the paragraph beginning on page 5, line 29 and ending on page 5, line 29 with the following amended paragraph:

~~Figure 22 shows~~ Figures 22(A), 22(B) and 22(C) show a synthetic pathway to prepare epothilone analogue **27D**.

Please replace the paragraph beginning on page 5, line 31 and ending on page 5, line 31 with the following amended paragraph:

~~Figure 23 shows~~ Figures 23(A), 23(B) and 23(C) show a synthetic pathway to prepare epothilone analogue **24D**.

Please replace the paragraph beginning on page 5, line 33 and ending on page 5, line 33 with the following amended paragraph:

~~Figure 24 shows~~ Figures 24(A) and 24(B) show a synthetic pathway to prepare epothilone analogue **19D**.

Please replace the paragraph beginning on page 5, line 35 and ending on page 5, line 35 with the following amended paragraph:

~~Figure 25 shows~~ Figures 25(A), 25(B), 25(C) and 25(D) show a synthetic pathway to prepare epothilone analogue **20D**.

Please replace the paragraph beginning on page 5, line 37 and ending on page 5, line 37 with the following amended paragraph:

~~Figure 26 shows~~ Figures 26(A), 26(B), 26(C) and 26(D) show a synthetic pathway to prepare epothilone analogue **22D**.

Please replace the paragraph beginning on page 6, line 1 and ending on page 6, line 2 with the following amended paragraph:

~~Figure 27 shows~~ Figures 27(A), 27(B) and 27(C) show a synthetic pathway to prepare epothilone analogue 12-hydroxy ethyl epothilone.

Please replace the paragraph beginning on page 6, line 4 and ending on page 6, line 7 with the following amended paragraph:

~~Figure 28 shows~~ Figures 28(A) and 28(B) show the activity of epothilone analogues in a sedimentation test in comparison with DMSO, epothilone A and/or B. Structures 17-20, 22, and 24-27 are shown in Figures 29-37, respectively. Compounds were added to tubulin (1 mg/ml) to

a concentration of 10 μ M. The quantity of microtubules formed with epothilone A was defined as 100%.

Please replace the paragraph beginning on page 6, line 30 and ending on page 6, line 32 with the following amended paragraph:

~~Figure 39 shows~~ Figures 39(A) and 39(B) show epothilone A and epothilone analogues #1-7. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

Please replace the paragraph beginning on page 6, line 34 and ending on page 6, line 36 with the following amended paragraph:

~~Figure 40 shows~~ Figures 40(A) and 40(B) show epothilone B and epothilone analogues #8-16. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

Please replace the paragraph beginning on page 7, line 1 and ending on page 7, line 3 with the following amended paragraph:

~~Figure 41 shows~~ Figures 41(A) and 41(B) show epothilone analogues #17-25. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

Please replace the paragraph beginning on page 7, line 5 and ending on page 7, line 7 with the following amended paragraph:

~~Figure 42(A) shows~~ Figures 42(A) and 42(B) show epothilone analogues #26-34. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

Please replace the paragraph beginning on page 7, line 10 and ending on page 7, line 12 with the following amended paragraph:

~~Figure 42(B) shows~~ Figures 42(C) and 42(D) show epothilone analogues #35-46. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

Please replace the paragraph beginning on page 7, line 14 and ending on page 7, line 14 with the following amended paragraph:

~~Figure 42(C)~~ Figure 42(E) shows epothilone analogues #47-49.